

**AMENDMENT AND RESPONSE TO OFFICE ACTION**

**Amendment**

**In the Specification**

Please amend the paragraph bridging pages 2 and 3 as follows.

Insulin, a polypeptide with a nominal molecular weight of 6,000 Daltons, traditionally has been produced by processing pig and cow pancreas to isolate the natural product. More recently, however, recombinant technology has been used to produce human insulin *in vitro*. Natural and recombinant human insulin in aqueous solution is in a hexameric configuration, that is, six molecules of recombinant insulin are noncovalently associated in a hexameric complex when dissolved in water in the presence of zinc ions. Hexameric insulin is not rapidly absorbed. In order for recombinant human insulin to be absorbed into a patient's circulation, the hexameric form must first associate dissociate into dimeric and/or monomeric forms before the material can move into the blood stream. The delay in absorption requires that the recombinant human insulin be administered approximately one half hour prior to meal time in order to produce therapeutic insulin blood level, which can be burdensome to patients who are required to accurately anticipate the times they will be eating. To overcome this delay, analogs of recombinant human insulin, such as HUMALOG<sup>TM</sup>, have been developed, which rapidly disassociate into a virtually entirely monomeric form following subcutaneous administration. Clinical studies have demonstrated that HUMALOG<sup>TM</sup> is absorbed quantitatively faster than recombinant human insulin after subcutaneous administration. See, for example, U.S. Patent No. 5,547,929 to Anderson Jr., et al.